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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/981,583	02/03/1998	ACHIM DICKMANNS	028622/0/0	8241

7590 06/18/2003

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[REDACTED] EXAMINER

HARRIS, ALANA M

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1642

DATE MAILED: 06/18/2003

39

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	08/981,583	DICKMANNS ET AL.
	Examiner Alana M. Harris, Ph.D.	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 21 March 2003.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,3-12,16-22,29-31,33-35 and 38-40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,3-12,16-22,29-31,33-35 and 38-40 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Claims 1, 3-12, 16-22, 29-31, 33-35, 38, 39 and 40 are pending.

Claims 1 and 16 have been amended.

Claim 2 has been cancelled.

Claims 1, 3-12, 16-22, 29-31, 33-35, 38, 39 and 40 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections

Claim Rejections - 35 USC § 103

3. All of the 35 U.S.C. 103(a) rejections set forth in Paper number 35, mailed November 22, 2002 have been withdrawn in light of Applicants' arguments.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 3-12, 16-22, 29-31, 33-35 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The

claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Newly amended claims 1 and 16 now include the recitation "wherein said cell was disseminated from primary tumor, has the phenotype of the primary tumor" and "wherein ...non-immortalized cell...has the phenotype of the primary tumor", respectively. Applicants have pointedly expressed where support can be found for this amendment. The Examiner has reviewed these sections of the specification and does not concur. On page 2, lines 31-34 suggests that there is a different expression of surface markers on the cells of the claimed invention as compared to the primary tumor cells. And on page 4, lines 28-32 the passage sets forth that the tumor cell of the claimed invention have conserved the phenotype of the residual tumor cells present. These citings are seemingly contradictory and do not support that the claimed cell as having the same phenotype as the primary tumor.

6. Claim 35 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants' claims read on the broad treatment of numerous epithelialy derived tumors with a therapeutically effective amount of an immortalized epithelial tumor cell.

Art Unit: 1642

Applicants' claims read on the broad treatment of numerous epithelial derived benign, semi-malignant or malignant neoplasms with a therapeutically effective amount of an immortalized epithelial tumor cell. Applicants' specification has not evidenced the use of an immortalized epithelial tumor cell in a method for treating any neoplasms *in vivo* or *in vitro*. Applicants have not provided any objective evidence (particularly *in vivo*, which the claims encompass) or data that supports the administration of immortalized epithelial tumor cell. The information provided in the specification is not substantive enough to support the claimed invention's effectiveness as a therapeutic. Further it is not clear how the cell would provide prevention of tumor. The specification fails to disclose enabling disclosure for use of an immortalized epithelial tumor cell as a therapeutic. The specification is silent in addressing which types of epithelial tumors are considered treatable using the said tumor. The specification does not exemplify any teachings of the implementation of the immortalized epithelial tumor cell in any cancer prevention or any parameters governing routes of administration, concentration of the immortalized epithelial cell medicament and times at which said treatment should take place. Since there are no teachings of the immortalized epithelial tumor cell as a therapeutic agent, Appellants' specification has not evidenced implementing these cells in therapies. Thus, the specification appears to present an invitation to experiment.

There is no guidance on the pharmacokinetics regarding any immortalized epithelial tumor cell to be administered, which is necessary for one of skill in the art to practice the invention in order to achieve predictable results. With regard to the results, in general, treatment of cancer is at most unpredictable as underscored by Gura

Art Unit: 1642

(Science 278: 1041 and 1042, November 7, 1997) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from *in-vitro* to *in-vivo* protocols, the problems of drug testing in knockout mice- particularly strains which have tumor suppressor gene knockouts, and problems of clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. The greatly increased complexity of the *in vivo* environment as compared to the very narrowly defined and controlled conditions of an *in vitro* assay does not permit a single extrapolation of an *in vitro* assay to human therapeutic efficacy with any reasonable degree of predictability. *In vitro* assays cannot easily assess cell-cell interactions that may be important in a particular pathological state. Further a therapeutic agent must accomplish several tasks to be effective: interact at the proper site of action, and it must do so at a therapeutic concentration and remain effective for a sufficient period of time. *In vitro* assays cannot duplicate the complex conditions of *in vivo* therapy.

Due to the unpredictability of therapeutics, the absence of any evidence concerning the effectiveness of the undefined composition comprising a plethora of enamel substances as a pharmacological agent, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the claimed invention with a reasonable expectation of success. The quantity of

experimentation necessary to determine whether or not an immortalized epithelial tumor cell is capable of preventing or treating any neoplasms is infinite.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. A review of *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed invention. These factors have been carefully considered in the instant grounds of rejection, and it is set forth that undue experimentation would be required by one of ordinary skill in the art to use the instant invention.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

Application/Control Number: 08/981,583

Page 7

Art Unit: 1642

308-4315 for regular communications and (703) 308-4315 for After Final
communications.

Any inquiry of a general nature or relating to the status of this application or
proceeding should be directed to the receptionist whose telephone number is (703) 308-
0196.



Alana M. Harris, Ph.D.
June 16, 2003